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Effect of crosslinking agents on poly(ethylmethacrylate) bone cements

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Asceptic loosening of cemented joint prostheses in many cases is related to the mechanical failure of the acrylic bone cement. Poly(methylmethacrylate) bone cements are widely used in orthopaedic surgery although there are well-known disadvantages. A lower modulus bone cement based on poly(ethylmethacrylate)–*n*-butylmethacrylate with a lower polymerization exotherm, and a low monomer extractibility, is a promising alternative. The effect of incorporating crosslinking agents in order to improve the mechanical performance of the PEMA bone cement is reported. Three different bifunctional dimethacrylate crosslinking agents with different chain lengths and degrees of flexibility were incorporated in the monomer phase, and cements formulated. The setting time was found to decrease in the presence of the cross-linking agents and the polymerization exotherm decreased in the presence of triethylene glycol dimethacrylate and polyethylene glycol dimethacrylate, $n = 400$. Incorporation of triethylene glycol dimethacrylate showed an increase in the tensile strength and modulus with a decrease in the strain at maximum stress. However, polyethylene glycol dimethacrylate, $n = 400$, did not improve the mechanical properties appreciably which may be attributed to the low crosslinking density and higher flexibility of the spacer group in the crosslinking agent.

1. Introduction

The use of polymeric bone cements in orthopaedics for the fixation of prostheses is associated with both beneficial and adverse effects. The bone cement acts as a grouting agent and aids in the immediate immobilization of the prostheses. A common problem in total hip replacement is the loosening of the cemented joint prostheses, which in many cases is related to mechanical failure of the acrylic bone cement [1–3]. Poly(methylmethacrylate) (PMMA) based bone cements are most commonly used in orthopaedics despite some well-known disadvantages. The major problems associated with the conventional PMMA cements are its high polymerization exotherm, low fracture resistance [4] and the use of methylmethacrylate monomer which has hypotensive effects. Improvements in PMMA cements have been focused towards use of particulate or fibre reinforcements [5–7] of the matrix. The addition of short carbon fibres [8] or inorganic fillers aid in reducing the creep of acrylic bone cements by increasing the stiffness and reducing the molecular mobility of the polymer chains. However, the addition of fibre or particulate fillers adversely affect the handling and manipulation of the cements and also give rise to poor intrusion characteristics and low fracture energy.

A reduced modulus acrylic bone cement based on poly(ethylmethacrylate)–*n*-butylmethacrylate (PEMA) [9] with a lower polymerization exotherm (~50 °C) and higher ductility has been reported as an alternative to PMMA. The monomer, *n*-butylmethacrylate, a higher analogue of methylmethacrylate is not irritant to soft tissue, is less toxic and is less extractable from the matrix. The PEMA cement is known to have a higher fracture toughness and superior fatigue life [10]. Although clinical trials of the PEMA cement have been generally satisfactory, there has been some incidence of polymer creep, leading to the loosening of the prostheses. In an effort to enhance the mechanical performance of the PEMA cement, particulate filler reinforcements have been effected with encouraging results [10]. The addition of inorganic filler, hydroxyapatite, improved the strength and modulus of the PEMA bone cements, especially on use of a

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silicated silanated hydroxyapatite [10]. A distinct problem, however, is the limitation of the amount of filler that can be incorporated without compromising handling characteristics.

In the present paper, the effect of crosslinking agents in the poly(ethylmethacrylate)–*n*-butylmethacrylate is reported. Crosslinking agents can be incorporated into linear polymers to improve properties such as stiffness and hardness [11]. The incorporation of crosslinking agents into a polymer may also improve physical properties, such as solvent resistance, toughness and shrinkage. Different crosslinking molecules may have different effects on mechanical and physical properties. In the present study, bifunctional dimethacrylates have been used as crosslinking agents in the monomer component with different chain lengths and degrees of flexibility. Three ethylene oxide adducts, ethylene glycoldimethacrylate (EGDMA), triethylene glycol dimethacrylate (TEGDMA) and poly(ethylene glycol dimethacrylate)$_n$, $n = 400$, were incorporated, which possess increasing length of spacer groups; the structures are shown in Fig. 1. The curing parameters and the mechanical properties are reported.

2. Materials and methods

PEMA and *n*-butylmethacrylate were procured from Bonar Polymers; triethylene glycol dimethacrylate (TEGDMA), ethylene glycol dimethacrylate (EGDMA), and poly(ethylene glycol)$_{n=400}$ dimethacrylate (PEGDMA), were purchased from Aldrich Chemicals and used without further purification. The liquid phase was modified by adding 2.0% and 5.0% wt/wt (with respect to polymer) of the corresponding crosslinking agent. The polymerization exotherms were recorded according to ASTM standard (F451) [12]. Tensile tests were carried out on an Instron at a crosshead speed of 5 mm min^{-1}. The control and experimental formulation of the bone cement were prepared using the conventional quantities, wherein a 2:1 polymer:monomer ratio is used.

The liquid component consisted of a 2.5% vol/vol DMPTA solution in *n*-butyl methacrylate monomer in all cases. The solid component consisted of PEMA beads and the liquid component was modified by adding 2.0% and 5.0% wt/wt (with respect to polymer) of the corresponding crosslinking agent in different experiments.

2.1. Polymerization exotherm

The exothermic polymerization temperatures were recorded according to ASTM standard (F451) [12]. The two components were mixed and approximately 25.0 g of the dough was packed into the plunger cavity of the mould. A thermocouple was positioned within its junction in the centre of the mould at a height of 3 mm in the internal cavity. The plunger was subsequently seated on the filled mould cavity and tightened with a G-clamp. Time was measured from onset of mixing the powder with liquid, and the temperature recorded. An average of two measurements were conducted as per the standard.

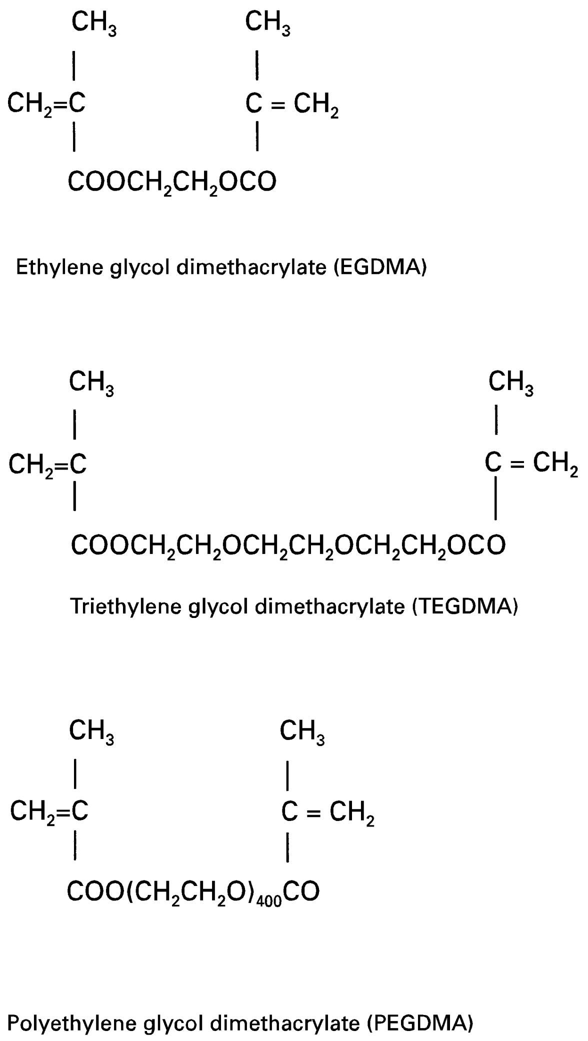

Figure 1 Chemical structures of the cross-linking agents.

2.2. Mechanical properties

Tensile tests of all specimens were carried out on an Instron machine with a cell load of 50 kN and at a crosshead speed of 5 mm min^{-1}. An extensometer was used to measure displacement. Specimens were prepared by placing the cement dough in PTFE moulds and subsequently placed under a pressure of 1.4 MPa for approximately 20 min. The specimens were then stored under dry conditions for 1 week before testing. Dumb-bell specimens were made in accordance to ISO-R527 and the average cross-section of the specimens was 5 mm × 4.0 mm. A minimum of six specimens were tested for each batch.

3. Results and discussion

The PEMA bone cement comprises of two phases which are the particles of the original polymer powder embedded in an interstitial matrix of a newly formed polymer. The polymerization of *n*-butyl methacrylate, in the presence of a crosslinking agent leads to the formation of a tridimensional network through crosslinkings. These crosslinks can provide anchoring points for the polymer chains and thus these anchor points are able to restrain excessive movement, maintaining the properties of the chains in the network. Formulations of PEMA bone cements were prepared by modifying the liquid component with the different crosslinking agents (Table I). The handling characteristics of each of the formulations were very similar to that of the parent PEMA formulation, and no problems were encountered in mixing of the cements. Figs 2–4 show the polymerization exotherms of the PEMA bone cement in the presence of EGDMA, TEGDMA and PEGDMA, respectively. The exotherms of each of the formulation were measured and the curves show the most representative curing parameters, peak temperature and setting time. The peak temperature is defined as the maximum temperature reached during the polymerization reaction, and the setting time can be determined according to the ASTM standard (F451), as the time when the temperature of the polymerizing mass is $T_{\text{amb}} + (T_{\text{max}} - T_{\text{amb}})/2$, where T_{max} is the maximum temperature (°C) and T_{amb} is the ambient temperature, 23 °C. The parent PEMA formulation had a polymerization exotherm of 50 °C and the addition of triethylene glycol dimethacrylate and polyethylene glycol dimethacrylate appreciably lowered the exotherm maximum which further decreased with increasing amounts of the crosslinking agent (Table II). As reported by Lautenschlager *et al.* [13], the amount of heat released is related to the quantity of the reacting monomer, whereas the temperature is dependent upon the rate at which it is dissipated. Ethylene glycol dimethacrylate increased the exotherm, indicating a high energy release during the crosslinking reaction; however, the setting time reduced in the presence of each of the different crosslinking agents at both concentrations.

The mechanical properties showed that the ultimate tensile strength increased with EGDMA and TEGDMA (Fig. 5) with increasing crosslinking density as compared to the uncrosslinked matrix. Theoretically, it can be expected that tensile strength with crosslinking will increase, as weak Van der Waals

TABLE I Concentrations of crosslinking agents

Crosslinking agent (% wt/wt)	EGDMA (mol %)	TEGDMA (mol %)	PEGDMA (mol %)
2.5	0.126	0.0087	0.0044
5.0	0.252	0.0175	0.0088

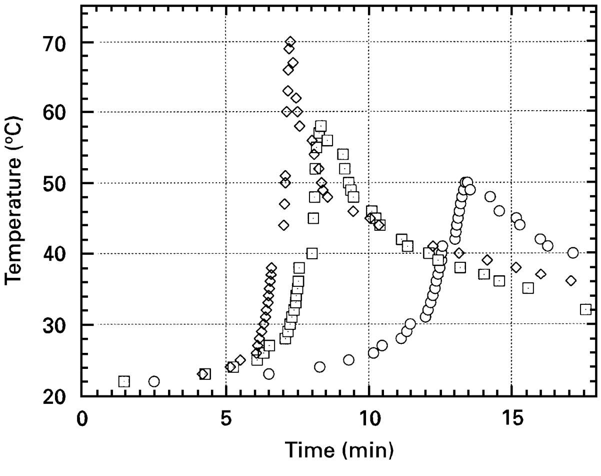

Figure 2 Comparison of the polymerization exotherms of (○) PEMA and PEMA with ethylene glycol dimethacrylate at (□) 2.5% and (◇) 5.0% by weight.

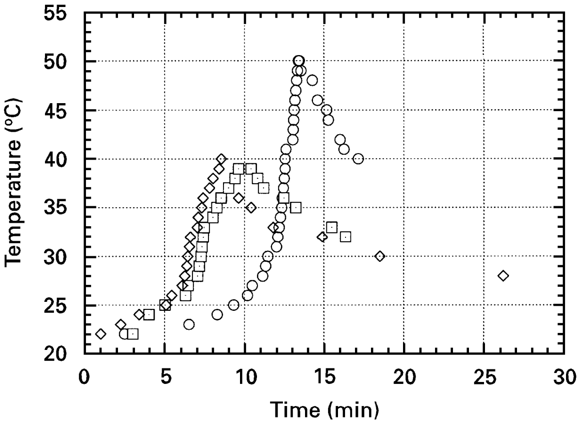

Figure 3 Comparison of the polymerization exotherms of (○) PEMA and PEMA with triethylene glycol dimethacrylate at (□) 2.5% and (◇) 5.0% by weight.

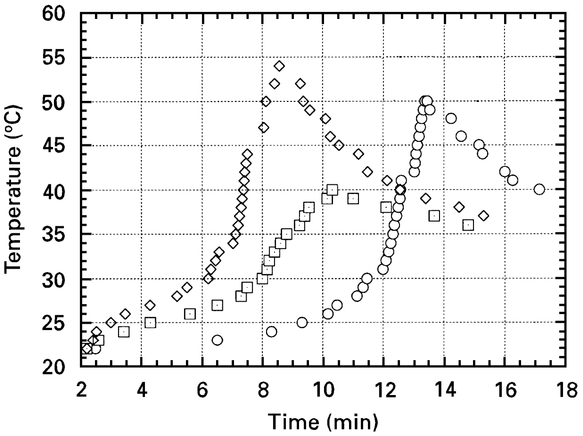

Figure 4 Comparison of the polymerization exotherms of (○) PEMA and PEMA with poly(ethylene glycol dimethacrylate) at (□) 2.5% and (◇) 5.0% by weight.

TABLE II Peak temperature and setting times of cements formulated with EGDMA, TEGDMA and PEGDMA

Bone cement	Exotherm (°C)	Setting time (min)
PEMA	50	11.8
PEMA + 2.5% EGDMA	55	6.8
PEMA + 5.0% EGDMA	69	6.2
PEMA + 2.5% TEGDMA	40	7.5
PEMA + 5.0% TEGDMA	39	6.5
PEMA + 2.5% PEGDMA	56	6.8
PEMA + 5.0% PGDMA	40	7.0

TABLE III Mechanical properties of the different PEMA-based cements in the presence of EGDMA, TEGDMA and PEGDMA

Cement	Ultimate tensile strength (MPa) [S.D.]	Young's modulus (GPa) [S.D.]	Strain at max stress (%) [S.D.]
PEMA	25.0 [0.2]	0.7 [0.21]	4.2 [0.0]
PEMA + EGDMA (2.5%)	24.5 [1.6]	1.35 [0.36]	3.8 [0.0]
PEMA + EGDMA (5.0%)	29.5 [1.6]	1.44 [0.14]	3.2 [0.0]
PEMA + TEGDMA (2.5%)	27.0 [0.28]	1.32 [0.14]	3.6 [0.1]
PEMA + TEGDMA (5.0%)	30.0 [0.51]	2.19 [0.37]	3.2 [0.0]
PEMA + PEGDMA (2.5%)	23.5 [0.53]	1.09 [0.39]	3.6 [0.28]
PEMA + PEGDMA (5.0%)	22.0 [1.08]	1.15 [0.28]	4.0 [0.3]

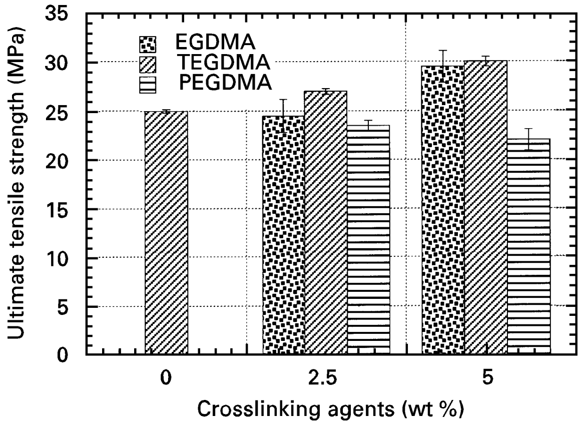

Figure 5 Variation of ultimate tensile strength in the presence of EGDMA, TEGDMA and PEGDMA.

forces of attraction are replaced by actual covalent bonds. Generally the effect of crosslinking agents influence the mechanical properties by the degree of crosslinking and by the copolymer effect. A comparison of the ultimate tensile strengths (Table III) shows an increase in the presence of EGDMA and TEGDMA, which increases further with increasing concentration of the crosslinking agents, thereby suggesting higher crosslinking density as expected. PEGDMA molecules, on the other hand, with its increasing length and higher flexibility of the spacer group did not improve the tensile strength in comparison to untreated PEMA cement. The low mole fraction (Table I) of PEGDMA, results in a low crosslinking density. The Young's modulus was found to increase with increasing crosslinking density in each of the formulations (Table III). The increase is a minimum in the case of PEGDMA, and may be due to the increasing number of flexible bonds between the two methacrylate groups, which then increases the chain mobility, rendering the network more flexible and thus lowering the modulus. In a similar study on PMMA bone cements [14], it was found that the use of PEGDMA at low mole fractions improved the tensile strength but did not increase the modulus due to the presence of the more flexible chains present. The strain at maximum stress was found to decrease in the presence of the crosslinking agents, as expected. As PEMA is a more ductile bone cement, the decrease in the strain with crosslinking is advantageous, unlike the PMMA cement where the existing brittleness is enhanced with crosslinking agents like EGDMA and TEGDMA [14]. The ductility decreased with increasing content of EGDMA and TEGDMA, i.e. with increasing crosslinking density, as expected. However, in the case of PEGDMA, although the crosslinking density increased with increasing feed content, simultaneously, the number of longer flexible crosslinks formed also increase, which affect chain mobility, thus lowering the strain at maximum stress at higher concentrations.

4. Conclusions

The use of crosslinking agents in the liquid component provided good handling characteristics and did not alter initial viscosities, as is observed in the case of particulate fillers. The polymerization of PEMA bone cements in the presence of crosslinking agents leads to the formation of a three-dimensional network, restraining excessive movement. The incorporation of TEGDMA at 5% by weight showed an increase in tensile strength and modulus. A comparison of the results show that increasing length and higher flexibility of the spacer group did not appreciably increase the tensile strength but lowered the strain at maximum stress of the system.

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